

Claims

I claim:

1. A peptide that is biologically active at melanocortin receptors comprising an AGRP(109-118) template and melanocortin agonist-based bioactive determinant sequences which have been substituted for the analogous template sequences, wherein
  - a) the melanocortin agonist-based bioactive determinant sequence is selected from the group consisting of:
    - i) Trp-Arg-Phe;
    - ii) Trp-Arg-DPhe;
    - iii) Phe-Arg-Trp;
    - iv) DPhe-Arg-Trp;
    - v) His-Phe-Arg-Trp; and
    - vi) His-DPhe-Arg-Trp.
  2. The peptide according to claim 1, wherein the peptide is of any SEQ ID NOS:4-7, 9, and 10.
  3. The peptide according to claim 1, wherein the melanocortin agonist-based bioactive determinant sequence includes at least one amino acid substituted within the sequence.
  4. The peptide according to claim 3, wherein the amino acid is selected from the group consisting of Ala; Atc; Bip; Lys; Nal(1'); Nal(2'); (pI)Phe; and Tic.
  5. The peptide according to claim 4, wherein the peptide is of any SEQ ID NOS:24-43.

6. The peptide according to claim 1, wherein the peptide further comprises a lactam bridge which is substituted for the disulfide bridge of the AGRP(109-118) template.

7. The peptide according to claim 6, wherein the peptide is of any SEQ ID NOS:2 and 11.

8. The peptide according to claim 6, wherein the peptide further comprises a second and a third bioactive determinant sequences at the N-terminal and C-terminal, respectively, wherein the second bioactive determinant sequence at the N-terminal is Ser-Tyr-Ser-Nle amino acid residues and the third bioactive determinant sequence at the C-terminal is Lys-Pro-Val amino acid residues.

9. A peptide that is biologically active at melanocortin receptors comprising a NDP-MSH linear tridecapeptide template and hAGRP(111-113) bioactive determinant sequences which have been substituted for the analogous template sequences, wherein

a) the hAGRP(111-113) bioactive determinant sequence is selected from the group consisting of:

- i) Arg-Phe-Phe;
- ii) Phe-Phe-Arg;
- iii) DArg-Phe-Phe;
- iv) Arg-DPhe-Phe; and
- v) Arg-Phe-DPhe.

10. The peptide according to claim 9, wherein the peptide is of any SEQ ID NOS:13-18.

11. A peptide that is biologically active at melanocortin receptors comprising a cyclic MTII heptapeptide template and hAGRP(111-113) bioactive determinant sequences which have been substituted for the analogous template sequences, wherein

a) the hAGRP(111-113) bioactive determinant sequence is selected from the group consisting of:

- i) Arg-Phe-Phe;
- ii) Phe-Phe-Arg;
- iii) DArg-Phe-Phe;
- iv) Arg-DPhe-Phe; and
- v) Arg-Phe-DPhe.

12. The peptide according to claim 11, wherein the peptide is of any SEQ ID NOS:20-23.

13. A pharmaceutical composition comprising a peptide that is biologically active at melanocortin receptors comprising an AGRP(109-118) template and melanocortin agonist-based bioactive determinant sequences which have been substituted for the analogous template sequences, and a pharmaceutically acceptable carrier or diluent, wherein

a) the melanocortin agonist-based bioactive determinant sequence is selected from the group consisting of:

- i) Trp-Arg-Phe;
- ii) Trp-Arg-DPhe;
- iii) Phe-Arg-Trp;
- iv) DPhe-Arg-Trp;
- v) His-Phe-Arg-Trp; and
- vi) His-DPhe-Arg-Trp.

14. The pharmaceutical composition according to claim 13, wherein the peptide is of any SEQ ID NOS:4-7, 9, and 10.

15. The pharmaceutical composition according to claim 13, wherein the melanocortin agonist-based bioactive determinant sequence includes at least one amino acid substituted within the sequence.
16. The pharmaceutical composition according to claim 15, wherein the amino acid is selected from the group consisting of Ala; Atc; Bip; Lys; Nal(1'); Nal(2'); (pI)Phe; and Tic.
17. The pharmaceutical composition according to claim 16, wherein the peptide is of any SEQ ID NOS:24-43.
18. The pharmaceutical composition according to claim 13, wherein the peptide further comprises a lactam bridge which is substituted for the disulfide bridge of the AGRP(109-118) template.
19. The pharmaceutical composition according to claim 18, wherein the peptide is of any SEQ ID NOS:2 and 11.
20. The pharmaceutical composition according to claim 18, wherein the peptide further comprises a second and a third bioactive determinant sequences at the N-terminal and C-terminal, respectively, wherein the second bioactive determinant sequence at the N-terminal is Ser-Tyr-Ser-Nle amino acid residues and the third bioactive determinant sequence at the C-terminal is Lys-Pro-Val amino acid residues.
21. A pharmaceutical composition comprising a peptide that is biologically active at melanocortin receptors comprising a NDP-MSH linear tridecapeptide template and hAGRP(111-113) bioactive determinant sequences which have been substituted for the analogous template sequences, and a pharmaceutically acceptable carrier or diluent, wherein

a) the hAGRP(111-113) bioactive determinant sequence is selected from the group consisting of:

- i) Arg-Phe-Phe;
- ii) Phe-Phe-Arg;
- iii) DArg-Phe-Phe;
- iv) Arg-DPhe-Phe; and
- v) Arg-Phe-DPhe.

22. The pharmaceutical composition according to claim 21, wherein the peptide is of any SEQ ID NOS:13-18.

23. A pharmaceutical composition comprising a peptide that is biologically active at melanocortin receptors comprising a cyclic MTII heptapeptide template and hAGRP(111-113) bioactive determinant sequences which have been substituted for the analogous template sequences, and a pharmaceutically acceptable carrier or diluent, wherein

a) the hAGRP(111-113) bioactive determinant sequence is selected from the group consisting of:

- i) Arg-Phe-Phe;
- ii) Phe-Phe-Arg;
- iii) DArg-Phe-Phe;
- iv) Arg-DPhe-Phe; and
- v) Arg-Phe-DPhe.

24. The pharmaceutical composition according to claim 23, wherein the peptide is of any SEQ ID NOS:20-23.

25. A method for treating in a patient a condition modulated by melanocortin receptors, the method comprising administering to the patient a pharmaceutical composition comprising a peptide that is biologically active at melanocortin receptors

comprising an AGRP(109-118) template and melanocortin agonist-based bioactive determinant sequences which have been substituted for the analogous template sequences, and a pharmaceutically acceptable carrier or diluent, wherein

a) the melanocortin agonist-based bioactive determinant sequence is selected from the group consisting of:

- i) Trp-Arg-Phe;
- ii) Trp-Arg-DPhe;
- iii) Phe-Arg-Trp;
- iv) DPhe-Arg-Trp;
- v) His-Phe-Arg-Trp; and
- vi) His-DPhe-Arg-Trp.

26. A method for treating in a patient a condition modulated by melanocortin receptors; the method comprising administering to the patient a pharmaceutical composition comprising a peptide that is biologically active at melanocortin receptors comprising a NDP-MSH linear tridecapeptide template and hAGRP(111-113) bioactive determinant sequences which have been substituted for the analogous template sequences, and a pharmaceutically acceptable carrier or diluent, wherein

a) the hAGRP(111-113) bioactive determinant sequence is selected from the group consisting of:

- i) Arg-Phe-Phe;
- ii) Phe-Phe-Arg;
- iii) DArg-Phe-Phe;
- iv) Arg-DPhe-Phe; and
- v) Arg-Phe-DPhe.

27. A method for treating in a patient a condition modulated by melanocortin receptors, the method comprising administering to the patient a pharmaceutical composition comprising a peptide that is biologically active at melanocortin receptors comprising a cyclic MTII heptapeptide template and hAGRP(111-113) bioactive

determinant sequences which have been substituted for the analogous template sequences, and a pharmaceutically acceptable carrier or diluent, wherein

a) the hAGRP(111-113) bioactive determinant sequence is selected from the group consisting of:

- i) Arg-Phe-Phe;
- ii) Phe-Phe-Arg;
- iii) DArg-Phe-Phe;
- iv) Arg-DPhe-Phe; and
- v) Arg-Phe-DPhe.